



PCT_US_10_579104_ST25.txt
SEQUENCE LISTING

<110> POLYPHOR LTD.
Universität Zürich

<120> Template fixed beta-hairpin mimetics and their use in phage display

<130> P1338US

<140> PCT/US 10/579104
<141> 2006-05-12

<150> PCT/EP 03/12783
<151> 2003-11-15

<160> 44

<170> PatentIn version 3.5

<210> 1
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<223> Key sequence known to occur in Platelet-Derived Growth Factor (PDGF), see Ross, R.; Raines, E. W.; Bowden-Pope, D.F.; Cell, 1986, 46, 155-159.

<400> 1
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<210> 2
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<212> PRT
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<220>
<223> Key sequence known to occur in Vasointestinal Peptide (VIP) showing neuroprotective properties against beta-amyloid neurotoxicity, see Proc. Natl. Am. Soc. USA, 1996, 96, 4143-4148.

<400> 2
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<220>
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<400> 3

Trp Leu Asp Val
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<210> 4
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<220>
<223> Key sequence known to occur in Factor Xa inhibitors, see Al
Obeidis, F.; Ostrem, J. A.; Drug Discovery Today, 1998, 3,
223-231.

<400> 4

Tyr Ile Arg Leu Pro
1 5

<210> 5
<211> 5
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<220>
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1463.

<400> 5

Tyr Ile Gly Ser Arg
1 5

<210> 6
<211> 5
<212> PRT
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<220>
<223> Key sequence known to occur in important physiologically active
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<400> 6

Ile Lys Val Ala Val
1 5

<210> 7
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<212> PRT
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<220>
<223> Key sequence known to occur in important physiologically active
peptides, see J. Biol. Chem., 1998, 273, 11001-11006 and
11007-11011.

<220>

<221> misc_feature
 <222> (4)..(5)
 <223> Xaa can be any naturally occurring amino acid
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Pro Pro Arg Xaa Xaa Trp
 1 5

<210> 8
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hairpin mimetic derived from the general formula Cys-Z-Cys wherein the alpha amino group of the first amino acid is acetylated and wherein Z consists of 8 amino acids.

<220>
 <221> DISULFID
 <222> (1)..(10)

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<400> 8

Cys Lys Trp Phe Leu Ala His Tyr Ala Cys
 1 5 10

<210> 9
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 8 amino acids, and wherein both R1 and R2 consist of 2 amino acids.

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<220>
 <221> DISULFID
 <222> (3)..(12)

<400> 9

Glu Thr Cys Lys Trp Phe Leu Ala His Tyr Ala Cys Thr Lys
 1 5 10

<210> 10
 <211> 12
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> hairpin mimetic derived from the general formula Cys-Z-Cys wherein the alpha amino group of the first amino acid is acetylated and wherein Z consists of 10 amino acids.

<220>
 <221> DISULFID
 <222> (1)..(12)

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<400> 10

Cys Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Cys
 1 5 10

<210> 11
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 <212> PRT
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<220>
 <223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 2 amino acids.

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<220>
 <221> DISULFID
 <222> (3)..(14)

<400> 11

Glu Thr Cys Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Cys Thr Lys
 1 5 10 15

<210> 12
 <211> 12
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hairpin mimetic derived from the general formula Cys-Z-Cys wherein the alpha amino group of the first amino acid is acetylated and wherein Z consists of 10 amino acids.

<220>
 <221> DISULFID
 <222> (1)..(12)

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<400> 12

Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys
 1 5 10

<210> 13
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 2 amino acids.

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<220>
 <221> DISULFID
 <222> (3)..(14)

<400> 13

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 1 5 10 15

<210> 14
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 2 amino acids.

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<220>
 <221> DISULFID
 <222> (3)..(14)

<400> 14

Asn Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Lys Val
 1 5 10 15

<210> 15

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2
 wherein the alpha amino group of the first amino acid is
 acetylated, wherein Z consists of 10 amino acids, and wherein
 both R1 and R2 consist of 2 amino acids.

<220>

<221> MOD_RES

<222> (1)..(1)

<223> ACETYLATION

<220>

<221> DISULFID

<222> (3)..(14)

<400> 15

Gly Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Gly Gly
 1 5 10 15

<210> 16

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2
 wherein the alpha amino group of the first amino acid is
 acetylated, wherein Z consists of 10 amino acids, and wherein
 both R1 and R2 consist of 2 amino acids.

<220>

<221> MOD_RES

<222> (1)..(1)

<223> ACETYLATION

<220>

<221> DISULFID

<222> (3)..(14)

<400> 16

Glu Thr Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Thr Lys
 1 5 10 15

<210> 17

<211> 18

<212> PRT
 <213> Artificial Sequence

<220>
 <223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 3 amino acids.

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<220>
 <221> DISULFID
 <222> (4)..(15)

<400> 17

Glu Leu Lys Cys Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Cys Glu
 1 5 10 15

Val Lys

<210> 18
 <211> 18
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 3 amino acids.

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> ACETYLATION

<220>
 <221> DISULFID
 <222> (4)..(15)

<400> 18

Lys Val Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Gly
 1 5 10 15

Leu Glu

<210> 19
 <211> 18
 <212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 10 amino acids, and wherein both R1 and R2 consist of 3 amino acids.

<220>

<221> MOD_RES

<222> (1)..(1)

<223> ACETYLATION

<220>

<221> DISULFID

<222> (4)..(15)

<400> 19

Gly Gly Gly Cys Thr Lys Trp Phe Leu Ala His Tyr Ala Thr Cys Gly
1 5 10 15

Gly Gly

<210> 20

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula Cys-Z-Cys wherein the alpha amino group of the first amino acid is acetylated and wherein Z consists of 12 amino acids.

<220>

<221> DISULFID

<222> (1)..(14)

<220>

<221> MOD_RES

<222> (1)..(1)

<223> ACETYLATION

<400> 20

Cys Gly Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Gly Cys
1 5 10

<210> 21

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Hairpin mimetic derived from the general formula R1-Cys-Z-Cys-R2 wherein the alpha amino group of the first amino acid is acetylated, wherein Z consists of 12 amino acids, and wherein

PCT_US_10_579104_ST25.txt
both R1 and R2 consist of 2 amino acids.

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> DISULFID
<222> (3)..(16)

<400> 21

Glu Thr Cys Gly Thr Lys Trp Phe Ser Asn His Tyr Gln Thr Gly Cys
1 5 10 15

Thr Lys

<210> 22
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Core peptide sequence Z taken from the CDR L3 loop of an antibody described in Jiang, L. et al., Chimia, 2000,54, 558-563.

<400> 22

Leu Trp Tyr Ser Asn His Trp Val
1 5

<210> 23
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified core peptide sequence Z derived from core peptide sequence with the SEQ ID NO:22 containing a stabilizing beta-turn and a beta-sheet sequence according to Chou, P. Y., Fasman, G. D., J. Mol. Biol, 1977, 115, 135-175.

<400> 23

Lys Trp Phe Ser Asn His Tyr Gln
1 5

<210> 24
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Core peptide sequence Z constructed from peptide with the SEQ ID NO:25.

<400> 24

Phe Leu Ala His Tyr Ala
 1 5

<210> 25

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Oligopeptide which does not contain a dedicated stabilizing
 beta-turn sequence or a beta-sheet sequence according to Chou, P.
 Y., Fasman, G. D., J. Mol. Biol, 1977, 115, 135-175.

<400> 25

Leu Trp Tyr Ser Asn His Trp Val Lys Trp
 1 5 10

<210> 26

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide No. 1 used to construct insert DNA coding for
 template fixed hairpin mimetic of SEQ ID NO:10 and used to
 construct insert DNA coding for randomized library template fixed
 beta-hairpin mimetics having sequences according to SEQ ID NO:42.

<400> 26

catgcccggg tacctttcta ttctcactct gaaacctgc

39

<210> 27

<211> 84

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide No. 2 used to construct insert DNA coding for
 template fixed hairpin mimetic of SEQ ID NO:10.

<400> 27

catgtttcgg ccgagccacc acctttggtg caggtctgat aatggttgct gaaccatttg

60

gtgcaggttt cagagtgaga atag

84

<210> 28

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> DNA sequence coding for the peptide shown in SEQ ID NO:8.

<400> 28

tgcaaatggt tcctggcgca ttatgcgtgc

30

<210> 29
 <211> 42
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:9.
 <400> 29
 gaaacctgca aatgggttcct ggcgcattat gcgtgcacca aa 42

<210> 30
 <211> 36
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:10.
 <400> 30
 tgcaccaaat ggttcagcaa ccattatcag acctgc 36

<210> 31
 <211> 48
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:11.
 <400> 31
 gaaacctgca ccaaattggtt cagcaaccat tatcagacct gcaccaaa 48

<210> 32
 <211> 36
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:12.
 <400> 32
 tgcaccaaat ggttcctggc gcattatgcg acctgc 36

<210> 33
 <211> 48
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:13.
 <400> 33
 ctggaatgca ccaaattggtt cctggcgcatt tatgcgacct gcaaagtt 48

<210> 34
 <211> 48

<212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:14.

 <400> 34
 aacggttgca ccaaatggtt cctggcgcac tatgcgacct gcaaagtt 48

 <210> 35
 <211> 48
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:15.

 <400> 35
 ggtggttgca ccaaatggtt cctggcgcac tatgcgacct gcggcggt 48

 <210> 36
 <211> 48
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:16.

 <400> 36
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 <210> 37
 <211> 54
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:17.

 <400> 37
 gaactgaaat gcaccaaatt gttcagcaac cattatcaga cctgcgaagt taaa 54

 <210> 38
 <211> 54
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> DNA sequence coding for the peptide shown in SEQ ID NO:18.

 <400> 38
 aaagttggtt gcaccaaatt gttcctggcg cattatgcga cctgcggtct ggaa 54

 <210> 39
 <211> 54
 <212> DNA
 <213> Artificial Sequence

PCT_US_10_579104_ST25.txt

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<220>
<223> DNA sequence coding for the peptide shown in SEQ ID NO:19.

<400> 39
gggtggtggct gcaccaaagt gttcctggcg cattatgcga cctgcggcgg tgggt          54

<210> 40
<211> 42
<212> DNA
<213> Artificial sequence

<220>
<223> DNA sequence coding for the peptide shown in SEQ ID NO:20.

<400> 40
tgcggtacca aatggttcag caaccattat cagaccggtt gc          42

<210> 41
<211> 54
<212> DNA
<213> Artificial sequence

<220>
<223> DNA sequence coding for the peptide shown in SEQ ID NO:21.

<400> 41
gaaacctgcg gtaccaaagt gttcagcaac cattatcaga ccggttgcac caaa          54

<210> 42
<211> 48
<212> DNA
<213> Artificial sequence

<220>
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<222> (10)..(11)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (13)..(14)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (16)..(17)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (28)..(29)
<223> n is a, c, g, or t

<220>
<221> misc_feature

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<222> (31)..(32)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (34)..(35)
 <223> n is a, c, g, or t

<220>
 <221> misc_feature
 <222> (37)..(38)
 <223> n is a, c, g, or t

<400> 42
 gaaacctgcn nknknknkcg tggtagacnnk nnknknknkt gcaccaaa

48

<210> 43
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Translated protein sequence of a randomized template fixed
 beta-hairpin mimetic phage library

<220>
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 <222> (3)..(14)

<220>
 <221> MISC_FEATURE
 <222> (4)..(6)
 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> MISC_FEATURE
 <222> (10)..(13)
 <223> Xaa can be any naturally occurring amino acid

<400> 43

Glu Thr Cys Xaa Xaa Xaa Arg Gly Asp Xaa Xaa Xaa Xaa Cys Thr Lys
 1 5 10 15

<210> 44
 <211> 84
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Oligonucleotide No. 3 used to construct insert DNA coding for
 randomized library template fixed beta-hairpin mimetics having
 sequences according to SEQ ID NO:42.

<220>
 <221> misc_feature
 <222> (34)..(35)
 <223> n is a, c, g, or t

<220>
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 <222> (40)..(41)
 <223> n is a, c, g, or t

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 <223> n is a, c, g, or t

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 <222> (55)..(56)
 <223> n is a, c, g, or t

<220>
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 <222> (58)..(59)
 <223> n is a, c, g, or t

<220>
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 <222> (61)..(62)
 <223> n is a, c, g, or t

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 nngcaggttt cagagtgaga atag 84